NRG Cancer Care Delivery Research Committee Meeting

Mary E. Cooley, PhD, RN, FAAN, CCDR Chair
Matthew Hudson, PhD, MPH, CCDR Vice-Chair

NRG Oncology Winter Meeting
February 11, 2022
NRG NCORP Cancer Care Delivery Research Priorities

Concepts/protocols focused on:

• Integrating patient-reported outcomes into clinical practice (extends survival);
• Enhance access to proven survivorship and palliative care strategies optimizing survivor and family quality of life;
• Optimize screening strategies based on disease risk including patients in the post-treatment surveillance phase of care; and
• Implement evidence-based symptom management strategies addressing patients’ needs during both active adjuvant and palliative treatment.
CCDR Announcements

Monthly CCDR committee meetings starting March 2022

• Opportunity to present your work and/or developing concept of interest

NCI webinars of interest

• Advancing rapid cycle research in cancer care, February 16-17, 2022
• Disparities among sexual and gender minority cancer survivors: Studies on prostate cancer among gay and bisexual men, February 15, 2022
• Webinar series: Telehealth and cancer: Studying its role in cancer control and care delivery, Monthly series from February 25, 2022-June 21, 2022
Landscape survey

Thank you to NRG CCDR committee members for participating in the development and review of landscape survey!

Melyssa Foust
Andrew McDonald
Nitin Ohri
Developing CCDR concepts

<table>
<thead>
<tr>
<th>Developing CCDR concepts and protocols</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Randomized Phase II Study of Physical Activity Monitoring to Enhance the Delivery of Definitive Radiotherapy for Locally Advanced NSCLC (NRG Foundation trial)</td>
<td>N. Ohri, MD</td>
</tr>
<tr>
<td>Exercise is Medicine in Medical Oncology</td>
<td>K. Schmitz, PhD; J. Trilk, PhD</td>
</tr>
<tr>
<td>Implementation of Guideline-based Molecular Profiling of Early-Stage Endometrial Cancer through NCORP/NRG Oncology</td>
<td>A. Hagemann, MD</td>
</tr>
<tr>
<td>Managing symptoms and psychological distress during oral anti-cancer tx</td>
<td>Alla Sikorski, PhD; Terry Badger, PhD</td>
</tr>
<tr>
<td>Implementation of <strong>A Toolkit to Address Persistent Chronic Cancer Pain Syndromes (ATACC)</strong></td>
<td>Jeannine Brant, PhD; Mary Cooley, PhD</td>
</tr>
<tr>
<td>Sexual orientation and gender identity (SOGI) measurement for patient centered cancer care in sexual and gender minority (SGM) populations</td>
<td>Megan Mullins, PhD</td>
</tr>
</tbody>
</table>
## Open NRG NCORP Trials

**accrual as of February 1, 2022**

<table>
<thead>
<tr>
<th>Study No</th>
<th>Disease Site</th>
<th>Description</th>
<th>Date Activated</th>
<th>Target Accrual</th>
<th>Total Accrual</th>
<th>NCORP Accrual (%)</th>
<th>Expected Closure Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRG-CC007CD</td>
<td>Prostate</td>
<td>Survivorship care plan for prostate cancer survivors on ADT to increase blood glucose and cholesterol checks in year 2 after starting ADT &amp; lower CVD risk</td>
<td>03/27/19</td>
<td>544</td>
<td>473</td>
<td>100%</td>
<td>April 2022</td>
</tr>
</tbody>
</table>
NRG-CC007CD NCORP Practices with Completed Enrollment

AnMed Health Cancer Center
CoxHealth Radiation Oncology
Geisinger Medical Center
Kaiser Permanente Northern California
MaineHealth Radiation Therapy
Medical Group of the Carolinas-Radiation Oncology
NCORP of the Carolinas
The University of Kansas Cancer Center
ATACCP: Effectiveness and Implementation of A Toolkit to Address Persistent Chronic Cancer Pain

Jeannine M. Brant, PhD, APRN, AOCN, FAAN
Mary E. Cooley, PhD, RN, FAAN
Patricia Ganz, MD
Disclosures

• None
Email solicitation to NCORP Contact PIs and Lead Research Associates (June 2021)
  - Initial e-mail contacts may have forwarded correspondence to individuals presumed better able to answer questions.

Respondents accessed survey via link (survey monkey)
  - Survey sent to 87 respondents
  - Response from 72 respondents
  - 82.7% response rate
Survey Questions

• Rank the top three symptoms for evidence-based symptom management *during* treatment (1st to 3rd)
• Rank the top three symptoms for evidence-based symptom management *post* treatment (1st to 3rd)
• Note supportive care management options available at [respondent’s] site
• Note the supportive care management option [respondent] uses
Ranked as number 1 symptom priority (n=72)
Ranked as a symptom priority (n=72)

Symptom priority (=72)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>During</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>70</td>
<td>0</td>
</tr>
<tr>
<td>Pain</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>CIPN</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>Depression</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Insomnia</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Sexual Function</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>
Problem of Cancer Pain

Chronic Cancer Pain

- Cancer pain is a significant problem throughout the cancer trajectory
- Persistent in 39.3% of patients following cancer treatment
  - Prevalence rates in real world data of specific pain syndromes is lacking
- Most efforts have focused on pain in patients with active disease
- Few studies exist that focus on managing cancer-related pain post-treatment

Types of Chronic Pain Syndromes

Post-Surgical Pain
- Post-mastectomy
- Post-thoracotomy
- Post-head/neck dissection

Chemotherapy-Induced Peripheral Neuropathy

Myalgias from Aromatase Inhibitors

Post-Radiation Pain Syndromes
- Plexopathies – brachial and lumbosacral

Variable presentation

Days

Weeks

Years

Challenges

Long-term Follow-up
• Number of cancer survivors anticipated to grow exponentially
• Need to optimize functioning and quality of life in post-treatment survivors
• Early identification of chronic and persistent pain essential

Lack of Consistent Assessment
• Lack of a tailored assessment to identify potential chronic pain syndromes

Lack of Knowledge
• Lack of knowledge and resources regarding approaches to management
• Fear of prescribing opioids in this potentially cured population

Objective

• Evaluate the effectiveness of an implementation-strategy guided pain assessment and management toolkit among patients with chronic cancer pain syndromes in post-treatment cancer survivors with breast, colorectal, head and neck, lung, and prostate cancers treated in NCORP community-based practices
Specific Aims

1. Determine the effectiveness of the ATACCp toolkit as measured by the 1) percentage of eligible patients who are screened for pain and 2) percentage of eligible patients that are referred to supportive care services for pain management between the intervention vs. usual care groups using a randomized cluster design.

2. Determine differences in pain severity levels and functional impairment between patients in the intervention vs. usual care groups using a randomized cluster design.

3. Examine the types of implementation strategies that are used by sites that are associated with increased uptake of the ATACCp toolkit.
Patient Inclusion Criteria

- Adult patients age 18 and older
- Cognitively intact; able to report pain and assessment parameters
- Diagnosed with breast, colorectal, prostate, lung, or head/neck cancer within the past 2 years
- Completed cancer treatment with curative intent within the past year
- Screen positive for a pain syndrome that is presumed to be attributed to receipt of cancer therapy (e.g. surgery, chemotherapy, radiation therapy)
- Pain intensity of $\geq 4$ during the past week
Site Inclusion Criteria

- Sites that treat and follow patients with breast, colorectal, prostate, lung, or head/neck cancer
- NCORP based practices
- Clinical champion on site to participate as part of study team
- May or may not have implemented patient-reported outcome measures
The pain assessment and management toolkit will include:

- A standardized pain assessment tool that can be integrated into the workflow processes
- A menu of multimodal pharmacologic and nonpharmacologic options, including supportive care/rehabilitation/physical therapy referrals, to manage pain with a focus on non-opioid strategies
- Help in identifying local resources for referrals
Implementation Strategies

Educational Webinars
- Chronic cancer pain syndromes
- Pain Assessment Tools
- Pharmacologic Management
- Nonpharmacologic Management

Chronic Pain Toolkit
- Menu of PROMIS measures
- Evidence-based pain management guidelines and checklists
- Pharmacologic strategies tailored to each pain syndrome
- Opioid downward titration guidelines
- Nonpharmacologic strategy options tailored to pain characteristics
- Quality improvement tools

Site Engagement
- Site Champions will serve as a liaison to lead and facilitate the study at each site
- Virtual site visits
- Welcome meeting
- Monthly Community of Practice meetings to share best practices
- Audit & Feedback sessions
Questions
Megan Mullins, PhD

Sexual orientation and gender identity (SOGI) measurement for patient centered cancer care in sexual and gender minority (SGM) populations
Sexual orientation and gender identity (SOGI) measurement for patient centered cancer care in sexual and gender minority (SGM) populations

Megan A. Mullins, PhD, MPH
NRG Oncology CCDR Meeting
February 11, 2022
Disclosures

• I have no disclosures to report.
Study Team

Megan Mullins, PhD, MPH, University of Michigan Rogel Cancer Center

Marina Stasenko, MD, Gynecologic Oncology, NYU Grossman School of Medicine

Co-Investigators
Lauren Wallner, PhD, MPH, University of Michigan Rogel Cancer Center
Mary Cooley, PhD, RN, FAAN, Dana Farber/ Harvard Cancer Center
Matthew Hudson, PhD, MPH, Prisma Health
Cancer Care for SGM Populations

- SGM were formally designated a health disparity population by National Institute of Health in 2016.

- Cancer disparities
  - Lower rates of cancer screening
  - Higher rates of certain cancers (anal, cervical, skin)
  - Later stages at diagnosis
  - Lower quality of cancer care
    - Patient-provider communication
    - Discrimination

A 2017 assessment found that only 1 in 5 NCORP practice groups routinely collect sexual orientation data, and only 1 in 10 routinely collect patient gender identity beyond male or female.
Sexual orientation measure

Do you think of yourself as:
• Lesbian, gay, or homosexual
• Straight or heterosexual
• Bisexual
• Something else (e.g. queer, pansexual, asexual)
• Don’t know
• Choose not to disclose
Gender identity measure

What is your current gender identity?
- Male
- Female
- Transgender man/transgender male
- Transgender woman/transgender female
- Other (e.g. non-binary, genderqueer, gender fluid, gender-diverse)
- Choose not to disclose

What sex were you assigned at birth?
- Male
- Female
**Aims of this Study**

**Aim 1:** To identify barriers and facilitators to SOGI measurement at the provider and system levels.

**Aim 2A:** To identify and prioritize implementation strategies to support SOGI measurement across NCORP sites.

**Aim 2B:** To refine intervention strategies and assess preliminary acceptability, feasibility, and appropriateness of identified strategies among a sample of targeted end users.
We are currently recruiting

10 Practice Sites
- 1 physician/ APRN/ PA
- 1 clinical staff member

20-30 minute Zoom interviews

Participants will be compensated with a $40 Amazon gift card for their time
How to participate

We are currently scheduling interviews with interested providers and staff at participating practices.

Erica Field will email a one-page information sheet after this meeting.

Email: mamull@umich.edu
Acknowledgements

Grant/Sponsor Acknowledgements

- T32-CA236621
- 5-UG1-CA-189867-08
References


Nitin Ohri, MD

NRG CCDR pilot project results: *Physical Activity Monitoring to Predict Hospitalization in Advanced Cancer Patients*
Physical Activity Monitoring to Predict Hospitalization in Advanced Cancer Patients

Nitin Ohri, MD, MS
Albert Einstein College of Medicine
Montefiore Medical Center
Department of Radiation Oncology
Why Study Wearables in Oncology?

Better selection of patients fit for treatment

Before Treatment

During Treatment

Improved evaluation of patients during treatment

Enhanced supportive care for patients with low activity levels

After Treatment

Enhanced monitoring for late toxicity or disease progression

Promoting healthful lifestyles in the survivorship period

Improved Clinical Outcomes

Reduced Health Care Expenditures

Improved Cancer Care Value

Improved Cancer Care Quality
# Activity Monitoring During Cancer Treatment at Montefiore/Einstein

<table>
<thead>
<tr>
<th>Trial</th>
<th>Disease Sites</th>
<th>Treatment</th>
<th>N</th>
<th>EORTC QLQ-C30</th>
<th>PRO-CTCAE</th>
<th>Wearable Device</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>Activity Monitoring Pilot</td>
<td>Head/Neck, Lung, GI</td>
<td>Concurrent chemoradiotherapy</td>
<td>38</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Completed, Published</td>
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<tr>
<td>Real-time Activity Monitoring to Prevent Admissions during RadioTherapy (RAMPART)</td>
<td>Head/Neck, Lung, Upper GI</td>
<td>Concurrent chemoradiotherapy</td>
<td>38</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Completed, Presented</td>
</tr>
<tr>
<td>A Simple Walking Program to Enhance Chemoradiotherapy Delivery</td>
<td>CNS, Head/Neck, Lung, GI, Cervix</td>
<td>Concurrent chemoradiotherapy</td>
<td>166</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Accrual completed</td>
</tr>
<tr>
<td>Activity Monitoring for Patients with Advanced Solid Tumors</td>
<td>Head/Neck, Lung, GI</td>
<td>Intravenous systemic therapy</td>
<td>60</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Accrual completed</td>
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<tr>
<td>Selective Personalized Radioimmunotherapy for NSCLC Trial (SPRINT)</td>
<td>NSCLC</td>
<td>Concurrent chemoradiotherapy versus pembrolizumab and radiotherapy</td>
<td>63</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Accrual completed</td>
</tr>
<tr>
<td>FLT3 Ligand, CD40 Agonist Antibody, and Stereotactic Radiotherapy versus Standard Therapy for Advanced Non-small Cell Lung Cancer: A Phase I/II Randomized Trial</td>
<td>NSCLC</td>
<td>Stereotactic radiotherapy and immunotherapy versus standard chemotherapy</td>
<td>46</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Open to accrual</td>
</tr>
<tr>
<td>PGHD Collection During Proton Chemoradiotherapy for Lung Cancer: A Pilot Study</td>
<td>Lung</td>
<td>Proton radiotherapy and concurrent chemotherapy</td>
<td>40</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Upcoming</td>
</tr>
<tr>
<td>NRGF-001: Activity Monitoring to Improve Patient Care during Chemoradiotherapy for LA-NSCLC</td>
<td>NSCLC</td>
<td>Concurrent chemoradiotherapy</td>
<td>144</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Upcoming</td>
</tr>
<tr>
<td>Selective Personalized Radioimmunotherapy for NSCLC Trial (SPRINT) 2</td>
<td>NSCLC</td>
<td>Pembrolizumab and radiotherapy +/- chemotherapy</td>
<td>36</td>
<td>X</td>
<td>X</td>
<td></td>
<td>Upcoming</td>
</tr>
</tbody>
</table>
Lessons so far

• Feasibility
  – Nearly all patients will agree wear a device
    • Most will keep it on
  – Few of our patients are willing to engage with a device

• Daily step counts are helpful
  – Easy to collect
  – Easy to interpret
  – Clinically relevant
    • Prognostic factor before treatment?
    • New vital sign during treatment?
Step Counts During Chemoradiotherapy and Hospitalization Risk

- Activity Monitoring Pilot Study
  - 14/38 subjects were hospitalized due to acute toxicities (triangles).
  - 38% reduction in the risk of hospitalization for every 1,000 steps taken each day (HR=0.62, p<0.001)
Prognostic Value of Baseline Activity Level in LA-NSCLC

• “Inactive” patients:
  – ↑ hospitalizations during RT
    • 50% v. 9%, p=0.004
  – ↓ rate of completing RT without delay >1 week
    • 67% v. 97%, p=0.006
  – ↓ PFS
    • median 5.3 months v. 18.3 months, HR=4.52, p<0.001
  – ↓ OS
    • median 15.0 months v. not reached, HR=3.88, p=0.007
3.1 Inclusion Criteria

- Age ≥ 18
- ECOG performance status 0-2
- Able to ambulate independently or with a cane (without the use of a walker)
- Planned or ongoing treatment with intravenous chemotherapy, intravenous immunotherapy, and/or intravenous targeted biologic therapy under the care of one of the study investigators and for one of the following diagnoses:
  - Metastatic head and neck cancer
  - Metastatic lung cancer (small cell or non-small cell), receiving 2\textsuperscript{nd}-line (or beyond) therapy for advanced disease
  - Metastatic gastric, esophageal, pancreatic, or hepatobiliary cancer
  - Metastatic colorectal cancer, receiving 2\textsuperscript{nd}-line (or beyond) therapy for advanced disease
- All patients must sign study specific informed consent prior to study entry.
# Physical Activity Monitoring to Predict Hospitalization in Advanced Cancer Patients

## 4.2 Study Calendar

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>At each visit in Medical Oncology or Radiation Oncology for six months</th>
<th>At visits in Medical Oncology or Radiation Oncology beyond six months</th>
</tr>
</thead>
<tbody>
<tr>
<td>History &amp; Physical Examination</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Toxicity Assessment</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>EORTC QLQ-C30</td>
<td>X</td>
<td>X*</td>
<td>(X*)</td>
</tr>
<tr>
<td>Activity Data Review</td>
<td>X</td>
<td>X</td>
<td>(X)</td>
</tr>
</tbody>
</table>

* - will not be completed more than once in a week.  
(X) – optional.

Wearable activity monitor (left) and wireless access client (right)
Physical Activity Monitoring to Predict Hospitalization in Advanced Cancer Patients

1.1 Primary Objective
- To demonstrate the feasibility of monitoring physical activity for patients with metastatic cancer who are receiving intravenous systemic therapy and providing that data to oncologists at each clinic visit.
  
  “feasibility” = collecting data at ≥80% of clinic visits

1.2 Exploratory Secondary Objectives
- To assess associations between daily step counts and adverse clinical events, including emergency room visits, hospitalizations, decline in quality of life, and death.
- To assess associations between daily step counts and markers of aggressive end of life care, including administration of chemotherapy within the last 14 days of life, initiation of advanced radiotherapy treatments within the last 30 days of life, and hospice enrollment at least 3 days before death.

Sample size: 60 subjects
Update

- 3/1/2018 – IRB Approval
- 12/13/2018 – Received funding from NRG CCDR Pilot Project Award
- 60 subjects enrolled between 3/28/2018 and 10/22/2021, 2 withdrew consent
  - 26 deaths
  - 38 subjects with hospitalizations
  - 38 subjects with ER visits
  - ≈400 med/rad onc visits within 6 months
    - Step data reviewed at ≈70% of visits
  - >6,000 days of step data collected

### Table

<table>
<thead>
<tr>
<th>Gender</th>
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<tbody>
<tr>
<td>Male</td>
<td>41</td>
</tr>
<tr>
<td>Female</td>
<td>19</td>
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<table>
<thead>
<tr>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Head and Neck Cancer</td>
<td>1</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>21</td>
</tr>
<tr>
<td>Esophageal Cancer</td>
<td>3</td>
</tr>
<tr>
<td>Gastric Cancer</td>
<td>4</td>
</tr>
<tr>
<td>Pancreatic Cancer</td>
<td>6</td>
</tr>
<tr>
<td>Primary Liver Cancer</td>
<td>15</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>8</td>
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</table>

<table>
<thead>
<tr>
<th>Systemic Therapy at Registration</th>
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<tbody>
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<td>IV Chemotherapy</td>
<td>33</td>
</tr>
<tr>
<td>IV Targeted therapy</td>
<td>8</td>
</tr>
<tr>
<td>IV Immunotherapy</td>
<td>27</td>
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</table>

<table>
<thead>
<tr>
<th>ECOG Performance Status</th>
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<tbody>
<tr>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
</tr>
</tbody>
</table>
Interim Results

“Inactive” = below 25th percentile based on age

“Very inactive” = below 10th percentile based on age
Questions?
Andrea Hagemann, MD

Implementation of guideline-based molecular profiling of early-stage endometrial cancer
Implementation of Molecular Profiling in Endometrial Cancer: An NRG Landscape Mixed Methods Study

Andrea R. Hagemann, MD, MSCI
Washington University in St. Louis School of Medicine

NRG Semi-Annual Meeting, CCDR Committee
Friday, February 11, 2022
Disclosures

- I have no financial disclosures
Mapping the Landscape of Molecular Profiling in Endometrial Cancer

• How close are we to uniform guideline-based care across the US?

• What are the barriers and facilitators to guideline-based molecular profiling for EC?

• Would implementing uniform guideline-based care result in treatment changes?
ProMisE Algorithm based on TCGA

Figure 1. The Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) Algorithm to assess a new endometrial cancer sample. First, mismatch-repair (MMR)-deficiency is evaluated with immunohistochemistry (IHC) against MSH6 and PMS2 proteins. Second, the Polymerase Epsilon (POLE) exounuclease domain is tested by sequencing exons 9–14. Lastly, IHC for p53 is performed to determine patients with normal expression (IHC score 1+) versus complete loss/null (IHC score 0) or accumulation (IHC score 2+). Reproduced with permission from [31].

Cancers 2021, 13, 1478. https://doi.org/10.3390/cancers13061478
These Classifiers May Change Upfront Management

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Molecular Classification Unknown</th>
<th>Molecular Classification Known</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td>• Stage IA endometrioid, grade 1–2, LVSI negative or focal</td>
<td>• Stage I–II POLE EDM endometrial carcinoma, no residual disease</td>
</tr>
<tr>
<td></td>
<td>• Stage IA endometrioid, grade 1–2, LVSI negative or focal</td>
<td>• Stage IA MMRd/p33 wt endometrioid carcinoma, low grade + LVSI negative or focal</td>
</tr>
<tr>
<td><strong>Intermediate</strong></td>
<td>• Stage IB endometrioid, grade 1–2, LVSI negative or focal</td>
<td>• Stage IB MMRd/p33 wt endometrioid carcinoma, low-grade + LVSI negative or focal</td>
</tr>
<tr>
<td></td>
<td>• Stage IA endometrioid, grade 3, LVSI negative or focal</td>
<td>• Stage IA MMRd/p33 wt endometrioid carcinoma, high-grade + LVSI negative or focal</td>
</tr>
<tr>
<td></td>
<td>• Stage IA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) without myometrial invasion</td>
<td>• Stage IA p53 abn and/or non-endometrioid without myometrial invasion</td>
</tr>
<tr>
<td><strong>High-intermediate</strong></td>
<td>• Stage I endometrioid, substantial LVSI, regardless of grade and depth of invasion</td>
<td>• Stage I MMRd/p33 wt endometrioid carcinoma + substantial LVSI, regardless of grade and depth of invasion</td>
</tr>
<tr>
<td></td>
<td>• Stage IB endometrioid, grade 3, regardless of LVSI status</td>
<td>• Stage IB MMRd/p33 wt endometrioid carcinoma, high-grade regardless of LVSI status</td>
</tr>
<tr>
<td></td>
<td>• Stage II</td>
<td>• Stage II MMRd/p33 wt endometrioid carcinoma</td>
</tr>
<tr>
<td><strong>High</strong></td>
<td>• Stage III–IVA with no residual disease</td>
<td>• Stage III–IVA MMRd/p33 wt endometrioid carcinoma with no residual disease</td>
</tr>
<tr>
<td></td>
<td>• Stage I–IVA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) with myometrial invasion, and with no residual disease</td>
<td>• Stage I–IVA p53abn endometrial carcinoma with myometrial invasion, with no residual disease</td>
</tr>
<tr>
<td><strong>Advanced</strong></td>
<td>• Stage III–IVA with residual disease</td>
<td>• Stage III–IVA with residual disease of any molecular type</td>
</tr>
<tr>
<td><strong>Metastatic</strong></td>
<td>• Stage IVB</td>
<td>• Stage IVB of any molecular type</td>
</tr>
</tbody>
</table>

European Society of Gynaecological Oncology (ESGO), European Society for Radiotherapy and Oncology (ESTRO), European Society of Pathology (ESP), lymphovascular space invasion (LVSI).
2022 NCCN Guidelines for Molecular Analysis of EC

PRINCIPLES OF MOLECULAR ANALYSIS

- Molecular analysis of endometrial carcinoma has identified four clinically significant molecular subgroups with differing clinical prognoses: POLE mutations, microsatellite instability-high (MSI-H), copy number low, and copy number high.\textsuperscript{13}

- Consider comprehensive genomic profiling via a validated and/or FDA-approved assay in the initial evaluation of uterine neoplasms.

- Ancillary studies for POLE mutations, mismatch repair (MMR)/MSI, and aberrant p53 expression are encouraged to complement morphologic assessment of histologic tumor type.\textsuperscript{14} See Figure 1: Pathology and Genomics in Endometrial Carcinoma (ENDO-A 3 of 4).

- Universal testing of endometrial carcinomas for MMR proteins is recommended (MSI testing if results equivocal).
  - Testing may be performed on the initial biopsy or D&C material or the final hysterectomy specimen.
  - MLH1 loss should be further evaluated for promoter methylation to assess an epigenetic mechanism.

- Genetic counseling, molecular analysis, and testing for all other MMR abnormalities is recommended.
  - For those who are MMR-intact/MSI-stable or those who have not been screened, but who have a strong family history of endometrial and/or colorectal cancer, genetic counseling and testing is recommended. (See Lynch Syndrome/HNPCC in the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal).

- Consider NTRK gene fusion testing for metastatic or recurrent endometrial carcinoma.

- Consider tumor mutational burden (TMB) testing through a validated and/or FDA-approved assay.\textsuperscript{15}
PRINCIPLES OF MOLECULAR ANALYSIS

FIGURE 1: PATHOLOGY AND GENOMICS IN ENDOMETRIAL CARCINOMA
(The decision to use molecular testing/classification depends on the availability of resources and the multidisciplinary team of each center).†

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‡Diagnostic algorithm for integrated genomic-pathologic classification of endometrial carcinomas.

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Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
**Survey Questions Mapped to Implementation Frameworks (CFIR and PRISM)**

**Table 1. Key contextual questions for stakeholders, mapped to the PRISM Domain.**

<table>
<thead>
<tr>
<th>PRISM Domain</th>
<th>Contextual Factors</th>
<th>Implementation Assessment Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organizational Characteristics</strong></td>
<td>- # Pathologists, Rad Oncs, Gyn Onc per site &lt;br&gt; - Pathologists’ reporting structure &lt;br&gt; - Site-specific gyn onc and radioplen oncology practices for early-stage EC (vaginal brachytherapy, pelvic RT or none)</td>
<td>- Site stakeholder assessments by qualitative and quantitative interviews to define current patterns of practice &lt;br&gt; - Time from Surgery to Pathology Report Signout &lt;br&gt; - Sample pathology report review of EC staging (5 per site) &lt;br&gt; - stage/histology/grade/demographics &lt;br&gt; MMR status (reported? yes/no and result) &lt;br&gt; p53 status &lt;br&gt; POLE status</td>
</tr>
<tr>
<td><strong>Patient Characteristics</strong></td>
<td>Site’s endometrial cancer patient demographics</td>
<td></td>
</tr>
<tr>
<td><strong>Implementation and Sustainability Framework</strong></td>
<td>- Specific policy/standardized processes &lt;br&gt; - Specific goals for POLE &lt;br&gt; - Hospital integrated reporting &lt;br&gt; - Sites’ leadership support of POLE &lt;br&gt; - Low payer commitment to POLE &lt;br&gt; - Current prioritizers for POLE &lt;br&gt; - Thematic changes in perspective over time</td>
<td>- Assessing the implementation and sustainability of POLE &lt;br&gt; - Competing forces of organizational readiness and sustainability &lt;br&gt; - Process evaluation for POLE for sites to serve as regional NGS sites for POLE &lt;br&gt; - Willingness to send out slides for POLE testing</td>
</tr>
<tr>
<td><strong>External Environment</strong></td>
<td>- Readiness/availability of POLE send-out testing site &lt;br&gt; - Site contracting negotiations</td>
<td>- Comparison of POLE testing at US academic sites to NCORP sites &lt;br&gt; - Site-specific surveys, matched to and compared with Lead Academic sites</td>
</tr>
</tbody>
</table>
We would next like to understand how you perceive the benefits of and barriers to molecular testing in early-stage endometrial cancer.

MMR/MSI, p53, and POLE together are part of an endometrial classification algorithm known as ProMIS, and are recommended as part of the NCCN guidelines. Are you familiar with this NCCN algorithm?

I have never heard of this I am aware of this I have this familiar with this

How confident are you that you would be able to successfully implement molecular testing?

Not at all confident Moderately confident Very confident

Obtaining MMR/MSI testing is currently recommended for all EC patients. For which patient populations do you think it is worthwhile or valuable to additionally obtain p53 and POLE status? (Select all that apply)

☐ High risk EC  ☐ High-intermediate risk
☐ EC Low-intermediate  ☐ Risk EC Low risk EC
☐ None of the above

ECNo 1 of the above. Is there any situation where you think it is worthwhile or valuable to obtain this status?

How much would having pathogenic POLE testing change your practice patterns?

Not at all A small amount Quite a bit

Having molecular testing information would help me counsel my patients.

Strongly disagree Neither agree nor disagree Strongly agree

This information helps me involve my patient’s preferences in decision making.

Strongly disagree Neither agree nor disagree Strongly agree

Molecular testing information would help me provide the appropriate treatment for my patients.

Strongly disagree Neither agree nor disagree Strongly agree
We Welcome Your Participation!

- Participant Recruitment by E-mail
  - Gyn Oncs
  - Rad Oncs
  - Pathologists
- Opportunity to invite other colleagues
- Invitation for a structured interview
- Gift card incentives for your time
Acknowledgements

Washington University in St. Louis School of Medicine
• Elise Wilson, MD, PGY3
• Ian Hagemann, MD, PhD, Gyn Pathologist
• Maura Kepper, PhD, Public Health Scientist, Qualitative Research Expert
• Regina Huang, Statistician

National/International Team
• Sarah Temkin, MD, Gyn Onc
• Kathy Han, MD, Rad Onc
• Jessica McAlpine, MD, Gyn Onc

Grant/Sponsor Acknowledgements
• WashU Center for Dissemination and Implementation Research/Institute for Public Health Pilot Grant
Questions

thank you!